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L7: Entry 15 of 16

File: USPT

Jan 30, 1990

DOCUMENT-IDENTIFIER: US 4897269 A

TITLE: Administration of drugs with multiphase liposomal delivery system

Detailed Description Text (20):

(d) including preservative or antioxidant agents (e.g., benzoic acid, methyl and propyl paraben, BHA, tocopherol, benzyl alcohol);

Detailed Description Paragraph Table (9):

	Materials
	Minoxidil Milled 2 g Butylated
Hydroxyanisole USP (BHA) 25 mg	Ethanol USP (95%) 50 ml Propylene Glycol USP 35 ml
Benzyl Alcohol NF* 4.5 ml	Stock Solution (CaCl.sub.2 8 mM solution) 415 ml Tween
80** 5.0 ml	*Not to be added to the 2% minoxidil liposome formulation without preservatives. * & **If Tween 80 and/or benzoyl alcohol are used they displace an equivalent volume of CaCl.sub.2 solution.

Current US Original Classification (1):

424/450

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L6 and antioxidant	16

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<u>L7</u>	L6 and antioxidant	16	<u>L7</u>
<u>L6</u>	L5 and 424/450.ccls.	29	<u>L6</u>
<u>L5</u>	liposome same (benzyl adj1 alcohol)	1048	<u>L5</u>
<u>L4</u>	L3 and 424/450.ccls.	46	<u>L4</u>
<u>L3</u>	liposome same (phenol or cresol)	1119	<u>L3</u>
<u>L2</u>	L1 and 424/450.ccls.	93	<u>L2</u>
<u>L1</u>	liposome same (phenol or cresol or benzyl)	2198	<u>L1</u>

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L6: Entry 25 of 29

File: USPT

May 11, 1993

DOCUMENT-IDENTIFIER: US 5209720 A

TITLE: Methods for providing localized therapeutic heat to biological tissues and fluids using gas filled liposomes

Detailed Description Text (19):

For storage prior to use, the liposomes of the present invention may be suspended in an aqueous solution, such as a saline solution (for example, a phosphate buffered saline solution), or simply water, and stored preferably at a temperature of between about 2.degree. C. and about 10.degree. C., preferably at about 4.degree. C. Preferably, the water is sterile. Most preferably, the liposomes are stored in a hypertonic saline solution (e.g., about 0.3 to about 0.5% NaCl), although if desired, the saline solution may be isotonic. The solution also may be buffered, if desired, to provide a pH range of pH 6.8 to pH 7.4. Suitable buffers include, but are not limited to, acetate, citrate, phosphate and bicarbonate. Dextrose may also be included in the suspending media. Preferably, the aqueous solution is degassed (that is, degassed under vacuum pressure) prior to suspending the liposomes therein. Bacteriostatic agents may also be included with the liposomes to prevent bacterial degradation on storage. Suitable bacteriostatic agents include but are not limited to benzalkonium chloride, benzethonium chloride, benzoic acid, benzyl alcohol, butylparaben, cetylpyridinium chloride, chlorobutanol, chlorocresol, methylparaben, phenol, potassium benzoate, potassium sorbate, sodium benzoate and sorbic acid. One or more antioxidants may further be included with the gas filled liposomes to prevent oxidation of the lipid. Suitable antioxidants include tocopherol, ascorbic acid and ascorbyl palmitate. Liposomes prepared in the various foregoing manners may be stored for at least several weeks or months. Liposomes of the present invention may alternatively, if desired, be stored in their dried, unsuspended form, and such liposomes also have a shelf life of greater than several weeks or months. Specifically, the liposomes of the present invention, stored either way, generally have a shelf life stability of greater than about three weeks, preferably a shelf life stability of greater than about four weeks, more preferably a shelf life stability of greater than about five weeks, even more preferably a shelf life stability of greater than about three months, and often a shelf life stability that is even much longer, such as over six months, twelve months or even two years.

Current US Cross Reference Classification (1):

424/450

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May 11, 1993

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